



mucopolidosis III gamma

Mucopolidosis III gamma is a slowly progressive disorder that affects many parts of the body. Signs and symptoms of this condition typically appear around age 3.

Individuals with mucopolidosis III gamma grow slowly and have short stature. They also have stiff joints and dysostosis multiplex, which refers to multiple skeletal abnormalities seen on x-ray. Many affected individuals develop low bone mineral density (osteoporosis), which weakens the bones and makes them prone to fracture. Osteoporosis and progressive joint problems in people with mucopolidosis III gamma also cause pain, which becomes more severe over time.

People with mucopolidosis III gamma often have heart valve abnormalities and mild clouding of the clear covering of the eye (cornea). Their facial features become slightly thickened or "coarse" as they get older. A small percentage of people with this condition have mild intellectual disability or learning problems. Individuals with mucopolidosis III gamma generally survive into adulthood, but they may have a shortened lifespan.

Frequency

Mucopolidosis III gamma is a rare disorder, although its exact prevalence is unknown. It is estimated to occur in about 1 in 100,000 to 400,000 individuals worldwide.

Genetic Changes

Mutations in the *GNPTG* gene cause mucopolidosis III gamma. This gene provides instructions for making one part (subunit) of an enzyme called GlcNAc-1-phosphotransferase. This enzyme helps prepare certain newly made enzymes for transport to lysosomes. Lysosomes are compartments within the cell that use digestive enzymes to break down large molecules into smaller ones that can be reused by cells. GlcNAc-1-phosphotransferase is involved in the process of attaching a molecule called mannose-6-phosphate (M6P) to specific digestive enzymes. Just as luggage is tagged at the airport to direct it to the correct destination, enzymes are often "tagged" after they are made so they get to where they are needed in the cell. M6P acts as a tag that indicates a digestive enzyme should be transported to the lysosome.

Mutations in the *GNPTG* gene that cause mucopolidosis III gamma result in reduced activity of GlcNAc-1-phosphotransferase. These mutations disrupt the tagging of digestive enzymes with M6P, which prevents many enzymes from reaching the lysosomes. Digestive enzymes that do not receive the M6P tag end up outside the cell, where they have increased activity. The shortage of digestive enzymes within lysosomes causes large molecules to accumulate there. Conditions that cause molecules to build up inside lysosomes, including mucopolidosis III gamma, are called

lysosomal storage disorders. The signs and symptoms of mucopolipidosis III gamma are most likely due to the shortage of digestive enzymes inside lysosomes and the effects these enzymes have outside the cell.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- ML IIIC
- mucopolipidosis III
- mucopolipidosis III, variant
- mucopolipidosis IIIC
- mucopolipidosis type III
- pseudo-Hurler polydystrophy

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Mucopolipidosis III Gamma
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1854896/>

Other Diagnosis and Management Resources

- GeneReview: Mucopolipidosis III Gamma
<https://www.ncbi.nlm.nih.gov/books/NBK24701>
- MedlinePlus Encyclopedia: Cloudy Cornea
<https://medlineplus.gov/ency/article/003317.htm>
- MedlinePlus Encyclopedia: Heart Valves
<https://medlineplus.gov/ency/imagepages/9380.htm>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>

- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Cloudy Cornea
<https://medlineplus.gov/ency/article/003317.htm>
- Encyclopedia: Heart Valves
<https://medlineplus.gov/ency/imagepages/9380.htm>
- Health Topic: Metabolic Disorders
<https://medlineplus.gov/metabolicdisorders.html>
- Health Topic: Osteoporosis
<https://medlineplus.gov/osteoporosis.html>

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Mucopolidoses Fact Sheet
<https://www.ninds.nih.gov/Disorders/All-Disorders/Mucopolidoses-Information-Page>

Educational Resources

- Disease InfoSearch: Mucopolidosis III Gamma
<http://www.diseaseinfosearch.org/Mucopolidosis+III+Gamma/8910>
- MalaCards: mucopolidosis iii gamma
http://www.malacards.org/card/mucopolidosis_iii_gamma
- Orphanet: Mucopolidosis type III
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=577

Patient Support and Advocacy Resources

- ISMRD: The International Advocate for Glycoprotein Storage Diseases
<http://www.ismrd.org/>
- Lysosomal Diseases New Zealand
<http://www.ldnz.org.nz/>
- National MPS Society
<http://mpssociety.org/mps/ml-ii-ml-iii/>
- National Organization for Rare Disorders (NORD)
<https://rarediseases.org/rare-diseases/pseudo-hurler-polydystrophy/>

- The Canadian Society for Mucopolysaccharide & Related Diseases Inc.
<http://www.mpsociety.ca/>
- The MPS Society (UK)
<http://www.mpsociety.org.uk/diseases/related-diseases/ml-iii/>

GeneReviews

- Mucopolipidosis III Gamma
<https://www.ncbi.nlm.nih.gov/books/NBK24701>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22mucopolipidosis+III+gamma%22+OR+%22Mucopolipidosis+Type+III%22+OR+%22Pseudo-Hurler+Polydystrophy%22+OR+%22Mucopolipidosis+III%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28mucopolipidosis+III+gamma%29+OR+%28mucopolipidosis+iii%5BTIAB%5D%29+OR+%28mucopolipidosis+type+iii%5BTIAB%5D%29+OR+%28pseudo-hurler+polydystrophy%5BTIAB%5D%29+OR+%28mucopolipidosis+iiic%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

OMIM

- MUCOLIPIDOSIS III GAMMA
<http://omim.org/entry/252605>

Sources for This Summary

- Cathey SS, Kudo M, Tiede S, Raas-Rothschild A, Bräulke T, Beck M, Taylor HA, Canfield WM, Leroy JG, Neufeld EF, McKusick VA. Molecular order in mucopolipidosis II and III nomenclature. *Am J Med Genet A*. 2008 Feb 15;146A(4):512-3. doi: 10.1002/ajmg.a.32193.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18203164>
- Encarnação M, Lacerda L, Costa R, Prata MJ, Coutinho MF, Ribeiro H, Lopes L, Pineda M, Ignatius J, Galvez H, Mustonen A, Vieira P, Lima MR, Alves S. Molecular analysis of the GNPTAB and GNPTG genes in 13 patients with mucopolipidosis type II or type III - identification of eight novel mutations. *Clin Genet*. 2009 Jul;76(1):76-84. doi: 10.1111/j.1399-0004.2009.01185.x.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19659762>
- Liu S, Zhang W, Shi H, Meng Y, Qiu Z. Three novel homozygous mutations in the GNPTG gene that cause mucopolipidosis type III gamma. *Gene*. 2014 Feb 10;535(2):294-8. doi: 10.1016/j.gene.2013.11.010. Epub 2013 Dec 6.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24316125>

- Persichetti E, Chuzhanova NA, Dardis A, Tappino B, Pohl S, Thomas NS, Rosano C, Balducci C, Paciotti S, Dominissini S, Montalvo AL, Sibilio M, Parini R, Rigoldi M, Di Rocco M, Parenti G, Orlacchio A, Bembi B, Cooper DN, Filocamo M, Beccari T. Identification and molecular characterization of six novel mutations in the UDP-N-acetylglucosamine-1-phosphotransferase gamma subunit (GNPTG) gene in patients with mucopolipidosis III gamma. *Hum Mutat.* 2009 Jun; 30(6):978-84. doi: 10.1002/humu.20959.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19370764>
- Pohl S, Tiede S, Castrichini M, Cantz M, Gieselmann V, Bräulke T. Compensatory expression of human N-acetylglucosaminyl-1-phosphotransferase subunits in mucopolipidosis type III gamma. *Biochim Biophys Acta.* 2009 Mar;1792(3):221-5. doi: 10.1016/j.bbadis.2009.01.009.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19708128>
- Raas-Rothschild A, Bargal R, Goldman O, Ben-Asher E, Groener JE, Toutain A, Stemmer E, Ben-Neriah Z, Flusser H, Beemer FA, Penttinen M, Olender T, Rein AJ, Bach G, Zeigler M. Genomic organisation of the UDP-N-acetylglucosamine-1-phosphotransferase gamma subunit (GNPTAG) and its mutations in mucopolipidosis III. *J Med Genet.* 2004 Apr;41(4):e52.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15060128>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735719/>
- Raas-Rothschild A, Cormier-Daire V, Bao M, Genin E, Salomon R, Brewer K, Zeigler M, Mandel H, Toth S, Roe B, Munnich A, Canfield WM. Molecular basis of variant pseudo-hurler polydystrophy (mucopolipidosis IIIC). *J Clin Invest.* 2000 Mar;105(5):673-81.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10712439>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC289169/>

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